UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,277	02/02/2005	Igor Shvets	1817-0150PUS1	9349

2292 7590 03/25/2009

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
03/25/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/500,277	SHVETS ET AL.	
	Examiner	Art Unit	
	ANN Y. LAM	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47-55 and 79-93* is/are pending in the application.

4a) Of the above claim(s) *79-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-55 and 90-93* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 47-51, 54 and 90-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bard, 5,580,523, in view of Dovichi et al., 5,567,294, and further in view of Chung, 6331073.

Bard discloses an integrated chemical synthesizer system that is modular in design, and allows for the use of one or more of the same type of reactor, or a variety of different types of reactors, each having microliter capacity. The reactors can be used individually, together, and interchangeably with one another can be thermal, electrochemical, catalytic, enzymatic, photochemical or hollow chamber type. The modular nature of the system, component parts, e.g., the reactors, flow channels, sensors, detectors, allows easy replacement and/or interchangeability of the component parts and provides for versatility. See column 2, lines 33-47, and column 4, lines 53-64. For example, it should be easier to scale-up reactions because one would simply add additional modules of exactly the same type to increase output. See column 2, lines 61-67.

Bard further discloses that the reactor design is developed to form a reactor chamber having an ID [which appears to refer to a dimension] less than 100 um. The chamber is covered and the unit mounted on an assembly board containing fluid conveying channels, with fastening means, to provide for flow to and from the reactor chamber. See column 3, lines 39-44. The plurality of interchangeable reaction vessels are capable of handling reaction volumes from about 1 nL up to about 10 uL. Column 3, lines 45-50.

There can be included flow control components such as pumps, flow channels, manifolds, flow restrictors, valves, etc., with necessary fittings that allow them to be sealed with the pre-arranged or selectively located flow channels or connectors. The reaction units, can be chip like. See column 4, lines 35-46, and column 6, line 67. An exemplary embodiment includes an assembly of different chips (60, 70, 100, see fig. 3) on a single assembly board 80), wherein the chips are respectively a reactor, a separator and an analyzer, and each include the requisite structures and components to perform the designated process, e.g., separation and analysis. See column 6, lines 34-40. The assembly board also has channels (81-84 which communicate with the channels of the chips. Capillary tubings for reactors, detectors, etc., may be assembled on a support board. See column 6, lines 41-52.

With respect to claims 47-49, the Bard reactors/chips are equivalent to Applicant's biochips (60, 70, 100), each with at least one microchannel (see chips in fig. 3; see also column 3, lines 45-50, describing the nanoliter and microliter reaction volumes), the microchannel having an inlet port at one end and outlet port at the other

end. The assembly board with the channels/capillaries (e.g., 81-84) are equivalent to Applicant's liquid delivery unit having a plurality of liquid delivery ports, one for connection to each biochip. The "necessary fittings" to allow a seal between the respective channels in the chips and assembly board (col. 4, lines 39-41) are equivalent to a connection means, and the fittings are releasable since it is disclosed that the chips/reactors can be used interchangeably with one another (col. 2, lines 39-41.) The channels/capillaries in the assembly board are equivalent to separate enclosed transfer conduits. Bard disclose that the transfer conduits transfer fluids from chip to chip (see figure 3.)

However, Bard does not disclose well(s) in which a releasable connection means provide for transfer of fluid between the well and a chip. Bard does not appear to disclose how fluids/reagents/samples are introduced into the chips in the first place, that is, other than through transfer from chip to chip. However, Dovichi et al. teach one method of doing so.

Dovichi et al. teach using capillary tubes (26) to transfer fluids from wells (30) to an analyzer (20). See column 3, lines 33-37 and column 5, lines 17-20. Conductive elements and an electric field may be used to move molecules (col. 5, lines 17-20) or other means such as mumps can be used (col. 7, lines 1-4.) The number of capillary tubes can vary, for example 96 capillaries in a 12 by 8 array may be used to interface with a 96 well microtiter plate, or other arrays can be designed as needed. See col. 7, lines 5-10.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide capillary tubes to transfer fluids from microtiter plate wells to the multiple chips in the Bard assembly, in order to provide the fluid reagents to the chips as necessary for a particular analysis, as taught by Dovichi et al. While Dovichi et al. do not disclose multiple chips, the skilled artisan would recognize that in modifying the Bard assembly to include capillaries to introduce reagents from microtitre plate wells, the capillaries, connected at one end to the wells of the microtiter plate, can be connected at the other end to more than just one chip in order to attain the same purpose of introducing reagents into the chips for performing an analysis. While Bard does disclose providing a cover (12) to close the upper surface of the reactor to produce the finished chip (col. 5, lines 37-39), the skilled artisan would recognize that providing capillaries for introducing fluid reagents from microtiter wells as taught by Dovichi et al. would not depart from the basic concept of the Bard invention, i.e., to produce a modular system with components, e.g., reactors, separation chambers, analyzers, etc., that are easily assembled (col. 5, lines 1-4.) And the skilled artisan would have reasonable expectation of success since it is within the skills of the ordinary artisan to utilize connections and valves, such as those discussed by Bard (col. 4, lines 35-46) as well as Dovichi et al. (col. 7, lines 1-4), to interconnect the modified assembly such that fluids can be transferred from one place to another, and channels can be closed, etc.

Moreover, as Applicant has not specified how the connection means is resealable, it is emphasized that the capillary tubes of Dovichi et al. are considered releasable to the extent that they are sealed during transfer of fluids, in order to

necessitate the flow of fluids. Moreover, in the combination of the teachings of Dovici et al. and Bard, the skilled artisan would have recognized that the valves and necessary fittings disclosed by Bard to provide for a seal (col. 4, lines 39-41) can be utilized such that the capillary tubes of Dovichi et al. also provide for a seal using such known components as valves and fittings.

While Bard discloses that flow control components such as pumps, flow channels, manifolds, flow restrictors, valves, etc., with necessary fittings allow them to be sealed with the pre-arranged or selectively located flow channels or connectors, can be included (column 4, lines 35-46, and column 6, line 67), Bard does not disclose that bidirectional flow of liquid along each of the microchannels may take place.

However Chung teach that microfluid may be filled into and driven in a microchannel with any driving mechanism, and that a bidirectional driving pump may be used to transport the microfluid in the microchannel (col. 2, lines 60-63.) It would have been obvious to the skilled artisan that any of various known pumping mechanisms, such as a bidirectional driving pump as disclosed by Chung, may be used as the pump generally disclosed by Bard.

As to claim 49, the top of each well is equivalent to a port.

As to claims 50 and 51, Bard teaches that the biochips can include flow channels, manifolds, valves, etc., as necessary for a particular purpose (col. 4, lines 35-46), that can be sealed with other flow channels or connectors. The skilled artisan would have recognized that each chip can be formed such that they have more than one inlet port and more than one outlet port, each capable of being connected to a different liquid

delivery unit, as necessary for transferring the requisite reagents to carry out a particular analysis. Such modifications are within the skills of the ordinary artisan as they are based on the same principles as taught by the references, i.e., transferring fluid from a microtiter well to a chip (as taught by Bard), in addition to capillaries that transfer fluid from one chip to another (as taught by Dovichi et al.) The skilled artisan would have reasonable expectation of success since flow control means such as pumps and valves are well known and are also suggested by Bard (col. 4, lines 35-46) as well as Dovichi et al. (col. 7, lines 1-4), and the above modifications involve providing the requisite capillaries and such flow control means.

As to claim 54, the disclosed Bard microchannel can be considered to be formed of two connected microchannels, one microchannel having an inlet (i.e., the opening at its proximal end) and an outlet port (i.e., the opening at its distal end), which is connected to the second microchannel at that microchannels inlet.

As to claims 90-92, Applicant claims that the bidirectional flow of the liquid along each the microchannels enables introduction and exchange of different liquids without the introduction of air bubbles. It is noted that Applicant does not state where such liquids are introduced and exchanged without introduction of air bubbles. In any case, while there is no disclosure by Bard, the skilled artisan would have recognized that capillary sized channels with very small dimensions allow for fluids to fill the channels without air bubbles. Moreover, use of valves, fittings and tubings to seal the microfluidic components to allow for fluids to fill the channels without air bubbles requires simple manipulation of well known components is well within the skills of the ordinary artisan,

and such is also disclosed in the Bard patent, in which it is disclosed flow control components such as pumps, flow channels, manifolds, flow restrictors, valves, etc., with necessary fittings that allow them to be sealed with the pre-arranged or selectively located flow channels or connectors (column 4, lines 35-46, and column 6, line 67), and capillary tubings for reactors, detectors, etc., may be assembled on a support board. See column 6, lines 41-52.

Claim 52 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bard, 5,580,523, in view of Dovichi et al., 5,567,294, and Chung, 6,331,073, as applied to claim 49 above, and further in view of Yon-Hin et al., 6,440,645.

Bard and Dovichi et al. has been discussed above. However, neither disclose a Y-shaped microchannel.

Yon-Hin et al. disclose a chip having microfluidic channels, including an embodiment with a Y-shaped channel (see figure 4). Providing such channel shape as disclosed by Yon-Hin in the Bard chip is well within the skills of the ordinary artisan for any of various reasons, such as allowing for the introduction of reagents from two different inlets. The skilled artisan would have reasonable expectation of success since forming such channels involves the same photolithography and micromachining methods discussed by Bard (see col. 5, lines 44-48) 4. See also discussion of photolithography in column 4, lines 65-66, in the Yon-Hin et al. reference.

Claims 53, 55 and 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bard, 5,580,523, in view of Dovichi et al., 5,567,294, and Chung, 6,331,073, and further in view of Parce et al., 5,942,443.

Bard in view of Dovichi et al. have been discussed above (see claim 47) which is equally applicable to claims 53 and 55. However, neither Bard nor Dovichi et al. disclose that the microchannel of the chip has at least one intermediate portion of which has a different cross-sectional area to that of the rest of the microchannel (claim 53), or that the transfer conduits have internal cross sectional area substantially greater than that of each microchannel (claim 55.)

Parce et al. teach microfludic devices and specifically disclose that flow resistance can generally be adjusted by adjusting channel length or width (col. 20, lines 6-7 and 12-14.) As to claim 53, the skilled artisan would have had knowledge regarding basic fluid dynamics as disclosed by Parce et al., and thus it is within the skills of the ordinary artisan to provide microchannels in the chip having an intermediate portion with a width (or cross-sectional area) that is different from the rest of the microchannel as may be desired for workable or optimum fluid flow. Likewise, as to claim 55, it is within the skills of the ordinary artisan to provide transfer conduits having internal cross sectional area substantially greater than that of each microchannels as may be desired for workable or optimum fluid flow.

As to claim 93, Applicant claims that the bidirectional flow of the liquid along each the microchannels enables introduction and exchange of different liquids without the introduction of air bubbles. It is noted that Applicant does not state where such liquids are introduced and exchanged without introduction of air bubbles. In any case, while there is no disclosure by Bard, the skilled artisan would have recognized that capillary sized channels with very small dimensions allow for fluids to fill the channels without air bubbles. Moreover, use of valves, fittings and tubings to seal the microfluidic components to allow for fluids to fill the channels without air bubbles requires simple manipulation of well known components is well within the skills of the ordinary artisan, and such is also disclosed in the Bard patent, in which it is disclosed flow control components such as pumps, flow channels, manifolds, flow restrictors, valves, etc., with necessary fittings that allow them to be sealed with the pre-arranged or selectively located flow channels or connectors (column 4, lines 35-46, and column 6, line 67), and capillary tubings for reactors, detectors, etc., may be assembled on a support board. See column 6, lines 41-52.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. Applicant argues that Bard does not describe the releasable connection means and that in Dovichi et al. the sample is transferred in one direction. This argument is not persuasive since it is the teachings of Dovichi et al. that provides modification to the

Bard device to include a releasable connection means. As for bidirectional flow, this is taught in the newly cited patent to Chung.

Applicant further contends that the types of experiments on cell adhesion of the present invention cannot be performed using the apparatus of Dovichi et al. This is not persuasive since this argument relates to intended use, while the claims at issue are directed to a device, and the claims are not recited such that the claimed device is structurally different or otherwise patentable over the prior art.

Applicant additionally argue that the capillaries of Dovichi et al. are not resealable means according to the present invention and they are permanently fixed at the biochip. Applicant assert that the resealable aspect is a feature of the present invention and is instrumental to sustain the assays to change liquids, and to avoid formation of the bubbles. This argument is not persuasive as Applicant has not specified how the connection means is resealable. Thus, the capillary tubes of Dovichi et al. are considered releasable to the extent that they are sealed during transfer of fluids, in order to necessitate the flow of fluids. Moreover, in the combination of the teachings of Dovici et al. and Bard, the skilled artisan would have recognized that valves and necessary fittings disclosed by Bard to provide for a seal (col. 4, lines 39-41) can be utilized such that the capillary tubes of Dovichi et al. also provide for a seal using such known components as valves and fittings.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/
Primary Examiner, Art Unit 1641